

# Signal Transduction

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Integrative Physiology and Pharmacology

## Introduction to Physiology (0501110) Spring 2013

Subject	Lecture No.	Lecturer	Pages in the 11 <sup>th</sup> edition. textbook	Pages in the 12 <sup>th</sup> edition textbook
Receptors: types and adaptation - Membrane or intracellular - Ion channels - G-protein - Enzyme linked - Intracellular - Second messengers - cAMP and cGMP, Phospholipid - Calcium calmodulin and IRS	1-2		910-915	886-891
Signal Transduction (Regulation of cellular machinery) Extracellular regulators: nervous, endocrine, paracrine and autocrine	3		934-936 962-963	910-912 940-941
Steroids: Their Signal Transduction And Mechanism Of Action, Thyroid hormones, Nitric Oxide	5		949 954	926-927 931

Textbook: Guyton Medical Textbook of Physiology By: Guyton and Hall 12<sup>th</sup> edition  
 Book Chapter **Cell Signalling Biology Michael J. Berridge**

# Objectives:

- Define first messenger (Hormones)
- List hormone types
- Describe receptor types
- Outline the hormone receptors interactions
- Describe second messenger mechanism of action
- List second messengers

# Signaling Overview

## 1. Introduction

A. Definitions

B. Components involved in signaling

C. Types of signaling

## 2. Types of Signaling Ligands - cell-surface vs. intracellular

## 3. Three Major Classes of Signaling Receptors

Ion Channel-linked

G protein-coupled receptors (GPRs)

Enzyme-linked receptors

Tyrosine-Kinase Receptors

Overview

Mechanism of activation

Different ways that TKRs can be activated

TKs that are non-covalently linked with receptors

## 4. Second Messengers: cAMP, cGMP, IP3 and DAG, Ca<sup>2+</sup>, PIP3

## 5. Signaling Cascades

A. Ras GTPase

B. Adaptor proteins with SH2 and SH3 domains

C. MAP kinase pathway

D. 5 different kinases activated by different cascades

E. JAK-STAT pathway

# Signaling Overview

## 1. Introduction

### A. Definitions

**Signaling:** Cell-cell communication via signals.

**Signal transduction:** Process of converting extracellular signals into intra-cellular responses.

**Ligand:** The signaling molecule.

**Receptors:** Bind specific ligands. Transmit signals to intracellular targets. Different receptors can respond differently to the same ligand.

### B. Components involved in signaling:

*Ligands*

*Receptors*

*Intracellular Signaling Proteins*

*Intermediary Proteins*

*Enzymes*

*Second Messengers*

*Target Proteins*

*Inactivating Proteins*

## Overview of Signal Transduction

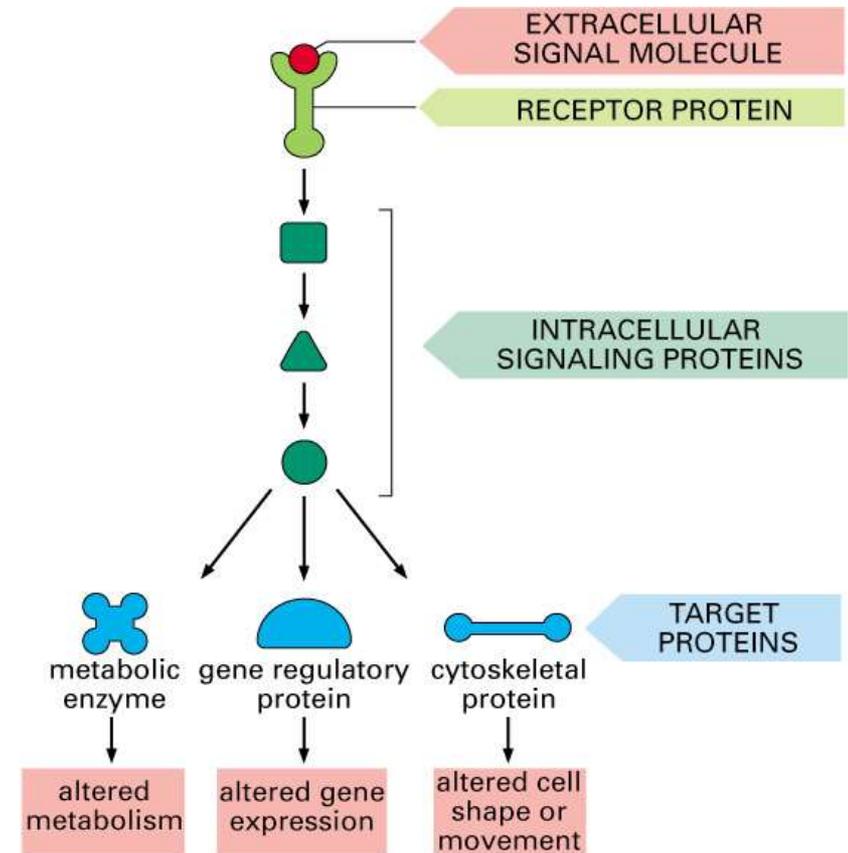
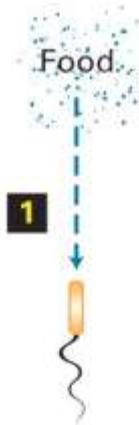
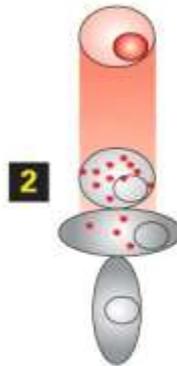


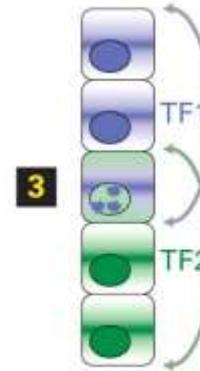
Figure 15-1. Molecular Biology of the Cell, 4th Edition.



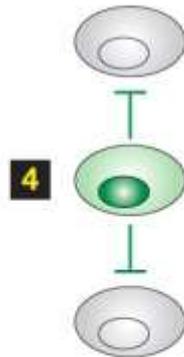
**1**  
Cells adjust to their particular environmental inputs (e.g., oxygen, sugar, and temperature)



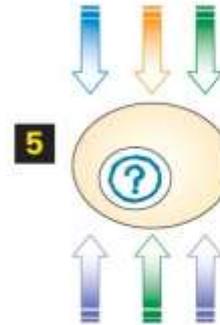
**2**  
Graded signals create different cell types



**3**  
Combined actions of transcription factors create different cell types



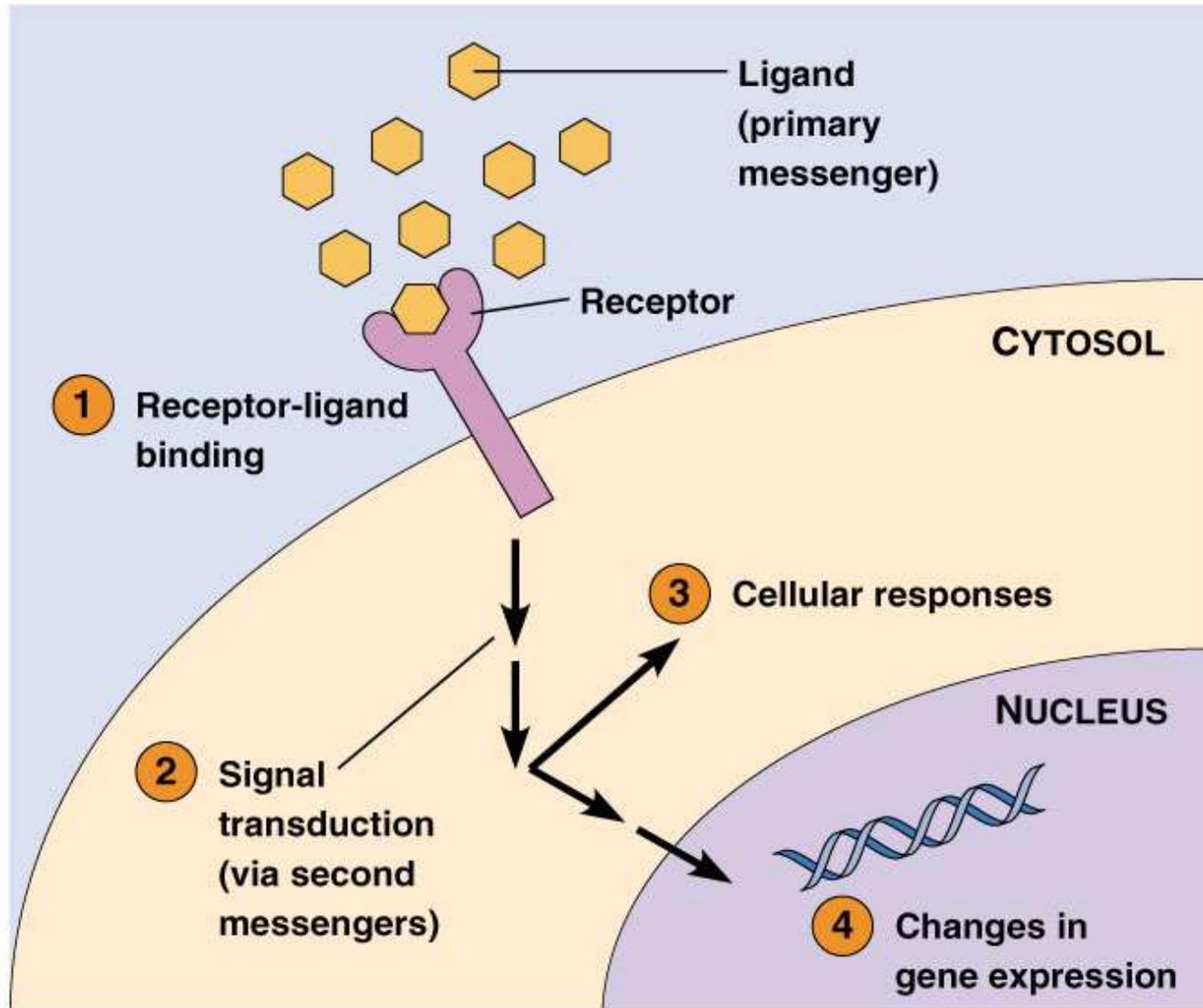
**4**  
Lateral inhibition signals prevent duplication of unique cell types

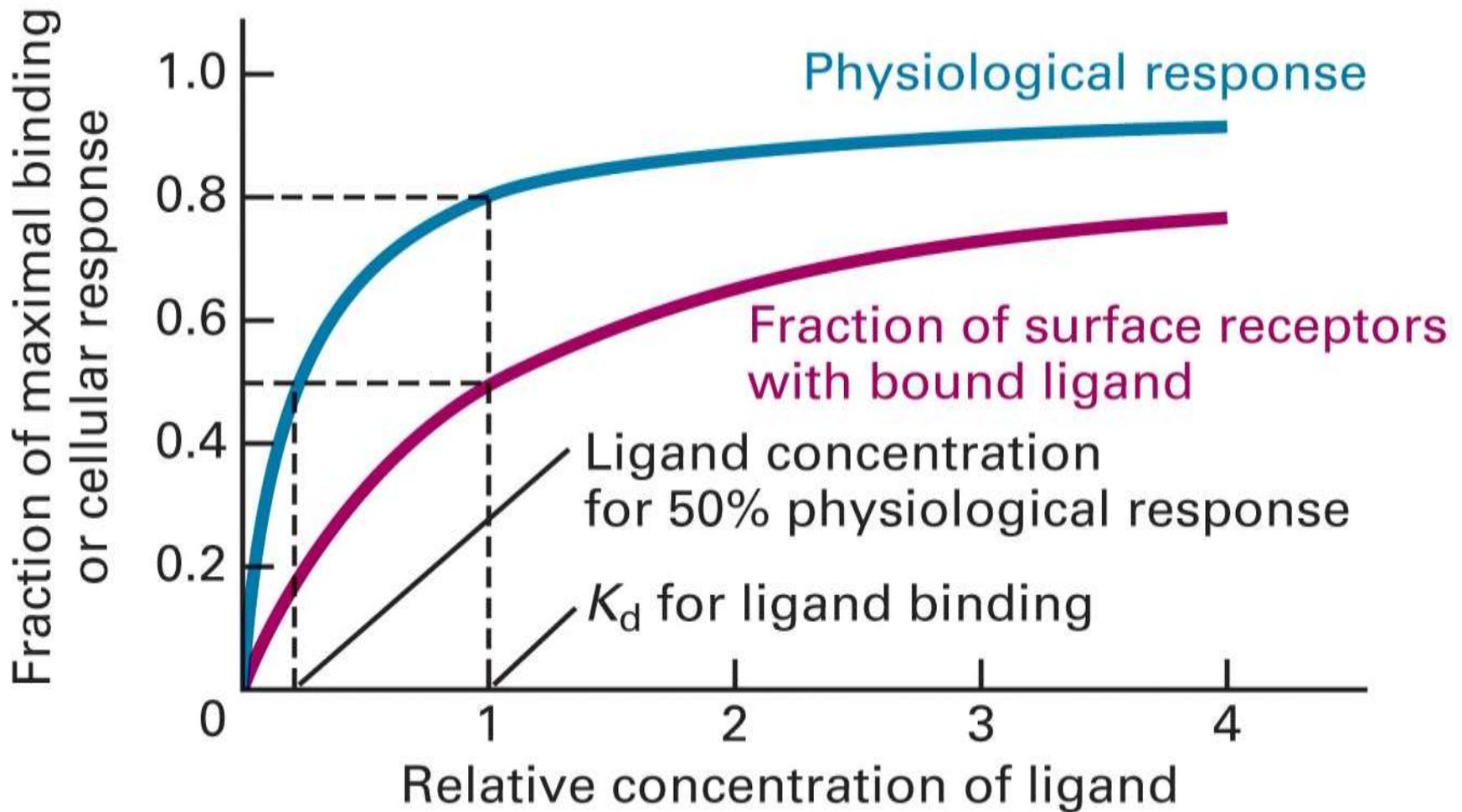


**5**  
Integration of signals allows cells to adjust to their neighbors and to change with time

Signaling is responsible for how cells can respond to their environment and how they can differentiate or change over time

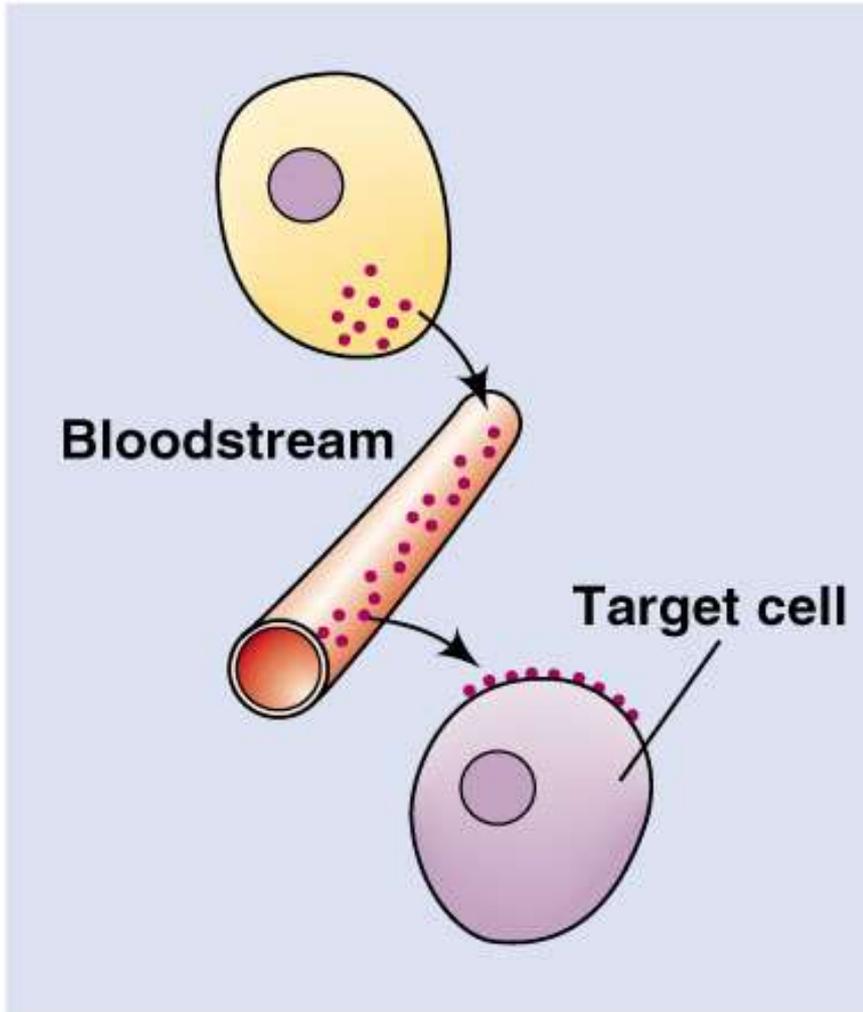
Signals get translated into cellular responses or changes in gene expression



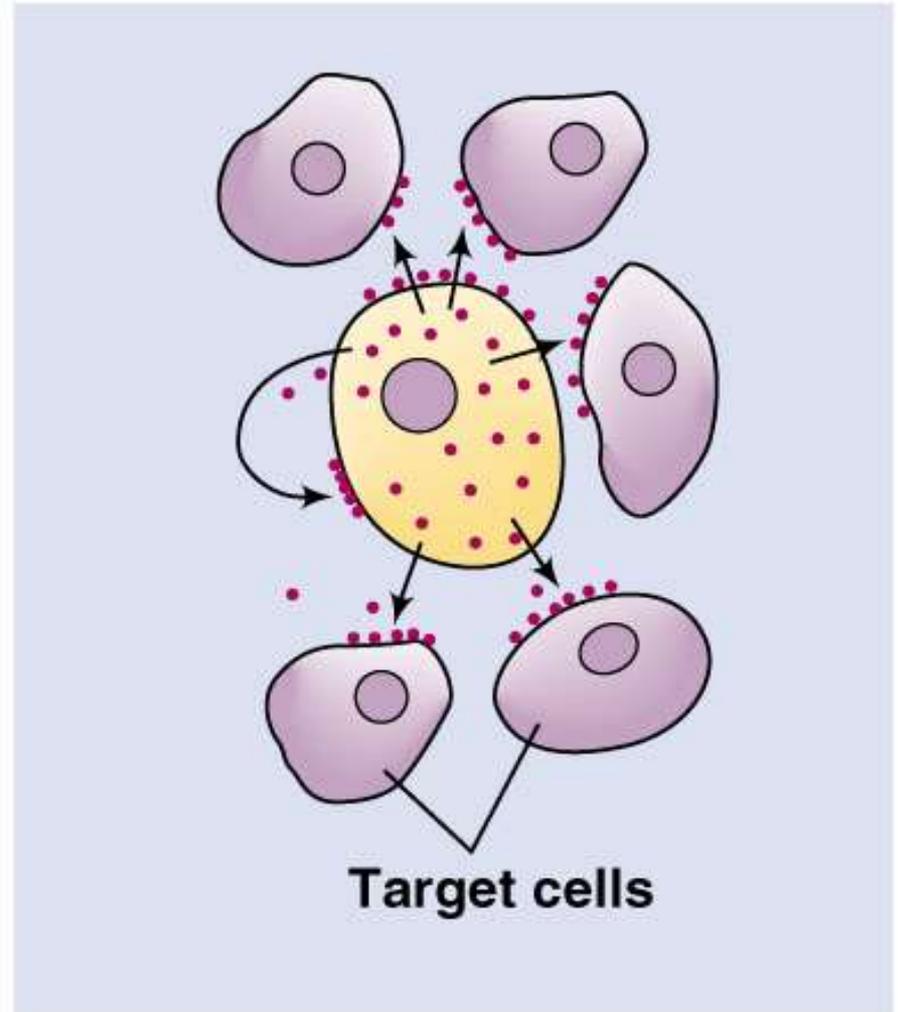


Not all of the receptor needs to be bound to induce a response

Signals can act locally or at a distance

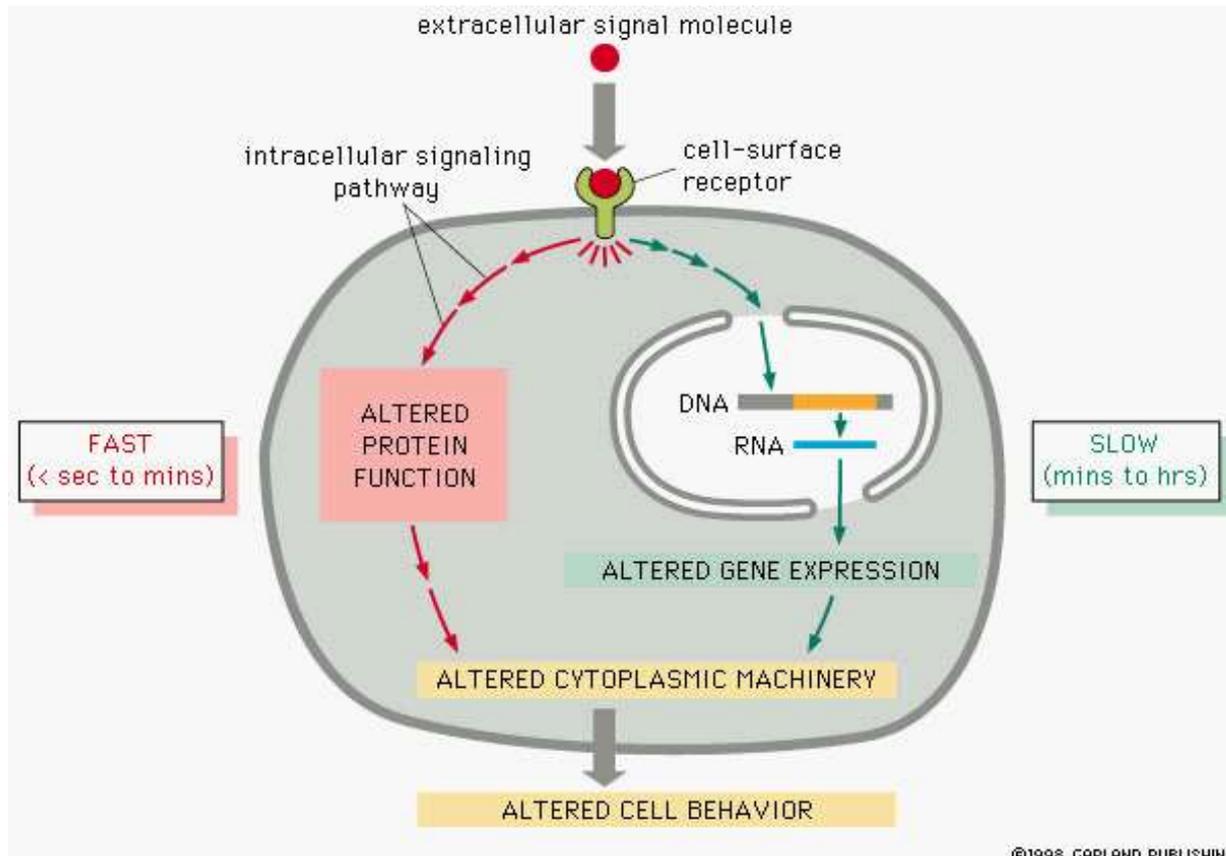


**Hormones**

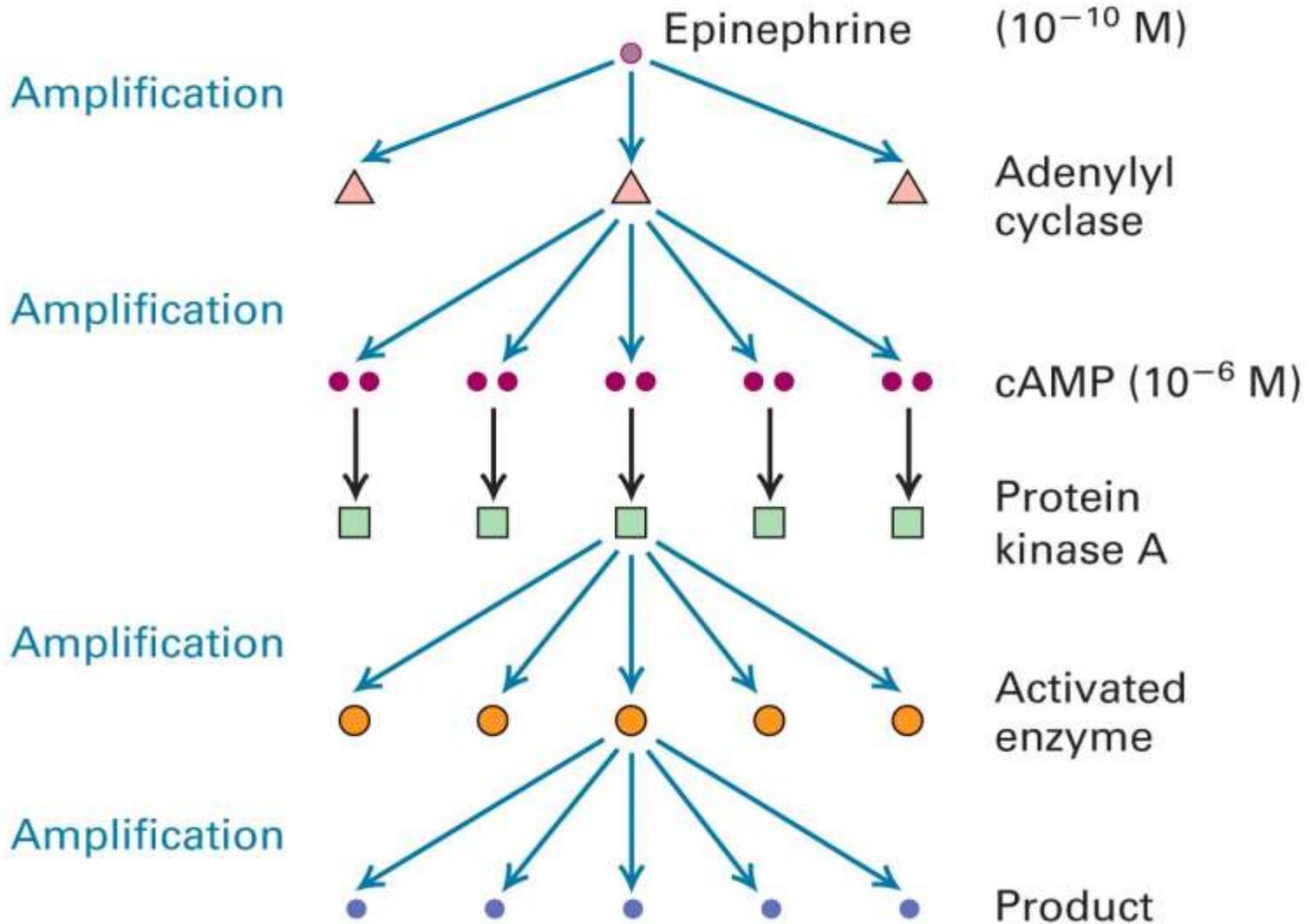


**Local mediators**

# Responses can be fast or slow



# Signals are amplified



# Signaling Overview

## 1. Introduction

### C. Types of signaling

i. Contact-dependent - via proteins in the PM:

ii. Via Secreted Signals:

- a. Autocrine - via growth factors, cell that releases the signal is also the target.
- b. Paracrine - via neurotransmitters and cytokines, action on adjacent target cells.
- c. Endocrine - via hormones, action on distant target cells.
- d. Synaptic - via neurotransmitters, action on post-synaptic cell in response to electrical stimuli

## 2. Types of Signaling Ligands:

### A. Ligands that bind to cell-surface receptors:

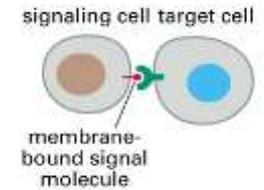
1. Neurotransmitters (NT), i.e. norepinephrine, histamine - hydrophilic (charged, polar)
2. Peptide hormones (P), i.e. insulin - can't cross membrane
3. Growth factors (GF), i.e. NGF, EGF, PDGF
4. Lipophilic signaling molecules, i.e. prostaglandins

### B. Ligands that bind to intracellular receptors:

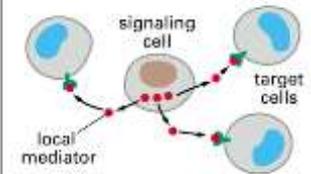
lipid soluble hormones that diffuse across the plasma membrane and interact with receptors in the cytosol or nucleus. i.e. steroids, thyroxine, retinoic acid, nitric oxide.

## Types of Signaling

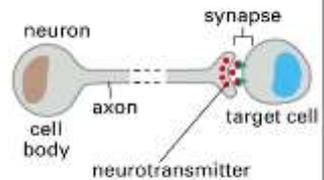
### (A) CONTACT-DEPENDENT



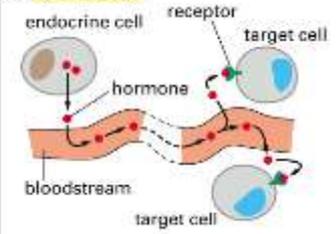
### (B) PARACRINE



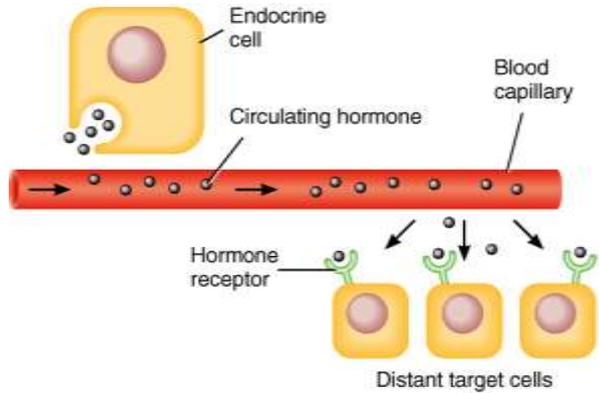
### (C) SYNAPTIC



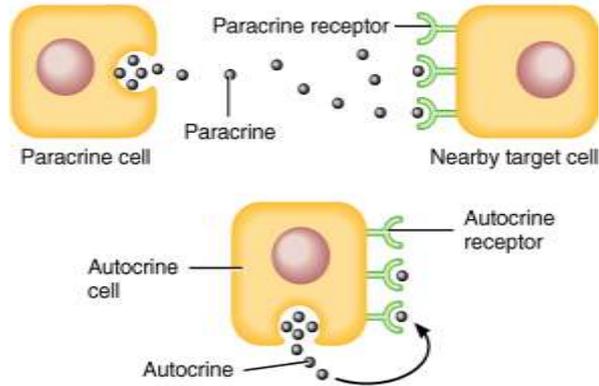
### (D) ENDOCRINE



# Local vs. Circulating hormones



(a) Circulating hormones



(b) Local hormones (paracrines and autocrines)

18.02

# Chemical classes of hormones

- ❑ Lipid-soluble hormones- use transport proteins in the **plasma**
  - ❑ Steroid: Lipids derived from cholesterol.
    - Are lipophilic hormones.
      - ❑ Testosterone.
      - ❑ Estradiol.
      - ❑ Cortisol.
      - ❑ Progesterone.
  - ❑ Thyroid ( amine but lipid soluble)
  - ❑ Nitric oxide (NO)

# Chemical classes of hormones

- ❑ Water-soluble – circulate in “free” form in the plasma
  - Amines:
    - ❑ Hormones derived from tyrosine and tryptophan.
  - Polypeptides and proteins:
    - ❑ Polypeptides:
      - Chains of < 100 amino acids in length.
        - ❑ ADH.
    - ❑ Protein hormones:
      - Polypeptide chains with > 100 amino acids.
      - Growth hormone.
  - Eicosanoid (prostaglandins) derived from arachidonic acid (20 carbon 4 double bonds)

# Chemical Classification of Hormones

- Glycoproteins:
  - Long polypeptides (>100) bound to 1 or more carbohydrate (CHO) groups.
    - FSH and LH, TSH and hCG (human chorionic gonadotropin)  
They have  $\alpha$  and  $\beta$  subunits ( $\alpha$  is common and  $\beta$  is specific)
- Hormones can also be divided into:
  - Polar:
    - H<sub>2</sub>O soluble.
  - Nonpolar (lipophilic):
    - H<sub>2</sub>O insoluble.
      - Can gain entry into target cells.
      - Steroid hormones and T<sub>4</sub> (thyroxine –tetraiodothyronine))